Clinical trial SUMMARY

Short study title

Study of S 81694 in perfusion in patients with solid tumours.

Full scientific title:

Phase I dose-escalation study of S 81694 administered intravenously in adult patients with advanced/metastatic solid tumours.

Therapeutic area:
Oncology

Indication:
Metastatic solid tumours

Study phase:
Phase 1

25th June 2020
Final version

In this summary:

1. Why was this study done?
2. When and where did this study take place?
3. Who participated in the study?
4. Which treatments did patients receive?
5. How was the study done?
6. What were the side effects?
7. What were the study results?
8. How has this study helped patients and researchers?
9. Are there plans for further studies?
10. Further information

CLINICAL TRIAL SUMMARY

Study of S 81694 in perfusion in patients with solid tumours

We would like to thank all the patients who participated in the study. As clinical study participants, they help researchers to discover new medicines for the benefit of all patients.

This document is a summary of the study. It is written for a general audience.

Researchers need many studies to decide which medicines work the best and are the safest for the patients. It involves a lot of people in many studies all around the world for medical science to progress. This summary only shows the results from this study. Other studies, evaluating the same drug, may find different results.

You should not change your current treatment based on the results of this single study. If you have any questions on this study, please speak to your doctor.

1 Why was this study done?

This study is called a "first-in-human phase 1" study. It means that it was the first time the test drug was given to human beings.
The study was done to assess the safety of a new anticancer drug in patients who had solid tumours that were locally advanced or had spread to other parts of the body. For those patients, the standard treatments were no longer effective or not suitable.
A solid tumour is an abnormal growth. These cancers can be in any organs of the body. They are different from cancer of the blood.
The current name of the study drug is S81694. MPS1 kinase is an enzyme that controls cell multiplication. S 81694 blocks the MPS1 kinase. This leads to cancer cells' death.
Researchers have expected that S81694 could be effective in patients with solid tumours.
The main objective of this study was to find the highest tolerated dose of treatment, called "maximum tolerated dose (MTD)". The MTD helps to find the dose that could be both safe and effective for patients.

2 When and where did this study take place?

When was it performed?

- This study started in September 2015.
- It ended in July 2019

Where did the study take place?

The study took place in the following countries:

Country	Number of patients included
Belgium	26
The Netherlands	13

3 Who participated in the study?

Which patients were included in the study?

Patients in the study had to meet notably the following criteria:

- Be 18 years of age or older.
- Diagnosed with any type of solid tumour that was locally advanced or had spread to other parts of the body.
- For whom standard treatments were no longer effective or not suitable.

In the study, the most frequent cancers were gastro-intestinal cancers, lung cancers and head and neck cancers.

How many patients participated in the study?

Overall 39 patients were enrolled in the study. One patient never received the treatment as the patient did not meet all inclusion criteria. Overall 38 patients had the treatment: 18 women and 20 men. All patients stopped the treatment, most of them because of the progression of their disease.

How old were the patients?

The average age of the patients was 58.7 years. The youngest patient was 44 years old and the oldest patient was 73 years old.

4 Which treatments did patients receive?

All patients received the same study drug called S81694.

Each patient received S81694 by intravenous (into a vein) infusion.
Patients received the drug during time periods called "cycles". A cycle lasted 28 days:

- Patients had one infusion of S81694 per week for 3 weeks.
- Then, there was 1 week without treatment.

This 28-day cycle was repeated if the cancer did not progress, and if the patient did not have too severe side effects.

5 How was the study done?

The study is called "open-label, dose escalation" study:

- "Open label" means that patients and doctors knew which treatment was given.
- "Dose escalation" means that different increasing doses of S81694 were tested.

To find the highest tolerated dose, different increasing doses of S81694 were tested one after the other in small groups of patients (3 to 7 patients).
During the study, 9 different doses levels were tested ranging from 4 mg to 135 mg.
For each dose, doctors checked if certain severe medical events called DLT (Dose Limiting Toxicity) occurred during the first treatment cycle. Those events could be caused by S81694.
Doctors were allowed to increase the dose for the next group of patients only if few of these severe medical events occurred.
The maximum tolerated dose (MTD) is the highest dose at which no more than a third of patients had DLT.

6 What were the side effects?

What about side effects?

Like all medicines, the study drug can cause side effects although not everybody gets them.
Side effects are unwanted events thought to be related to the treatments in the study (S81694).

The table below shows the number of treated patients who experienced side effects (adverse events considered as related to S81694 by the doctors).

	Number of patients
Patients who had side effect(s)	30 patients (79%)
Patients who had serious* side effect(s)	3 patients (8%)
Patients who withdrew because of side effect(s)	1 patient (3%)

**See definition below*

Overall 3 patients had dose limiting toxicity (severe medical events that doctors checked in order to decide if they could increase the dose or not).
The 3 events happened at 3 different doses and were: severe decrease in the number of red blood cells, severe high blood pressure crisis and severe tiredness.

How many patients had serious side effects?

A side effect is serious when:

- The patient needs to be hospitalized.
- The patient's life is in danger.
- Or it may put at risk the patient and requires a medical intervention to prevent the situations listed above.
- It causes permanent damage or death.

In this study, 3 patients (8%) had one serious side effect each (adverse event considered as related to S81694): diarrhoea, eye inflammation and high blood pressure crisis.
Overall, 1 patient withdrew because of a side effect which was the serious eye inflammation.
In this study, no patient died because of an unwanted event thought to be related to the study drug.

What were the other side effects?

The table below shows the other side effects reported in the study. Only the most common (reported by at least 3 patients) are presented.

	Number of patients
Decrease in the number of red blood cells	14 patients (37%)
Tiredness	11 patients (29%)
Feeling sick	8 patients (21%)
Decreased appetite	6 patients (16%)
Lack of white blood cells called neutrophils	5 patients (13%)
Diarrhoea	4 patients (11%)
Vomiting	3 patients (8%)
Headache	3 patients (8%)

7 What were the study results?

Preliminary study results did not show an effectiveness of S81694 when used alone. The sponsor decided to stop the development of S81694 as a single agent. The study was discontinued, and the maximum tolerated dose was not found. The decision to discontinue the study was not due to any safety reason.

8 How has this study helped patients and researchers?

This study helped researchers in their understanding of the study drug. Unfortunately, the use of S81694 alone does not seem to be effective in solid tumours. Findings from this study will help to learn whether S81694 can be useful in combination with other treatments.

9 Are there plans for further studies?

A clinical study with S81694 in combination with another anti-cancer drug has also been performed. The study terminated a short while ago. This study checked the safety of S81694 in combination with another anti-cancer drug.

10 Further information

What is the identification number of the clinical study?

- Protocol Number: CL1-81694-001
- EudraCT Number: 2014-002023-10
- ISRCTN35641359

Who did the study?

The company that organized and funded the research study, called sponsor, is the Institut de Recherches Internationales Servier based in Suresnes, France.

How can you contact the sponsor?

Contact us on Servier website (www.servier.com).

Where can you learn more about this study?

- The scientific summary is also available on Servier Clinical Trial Data website. (clinicaltrials.servier.com)
- In this document, we translated medical terms into lay terms. You can find the corresponding medical terms in the Servier glossary on Servier Clinical Trial Data website

In accordance with the recommendations of the Cancer Plan III (Measure 5.4), this document was submitted for review, and guidance to Clinical Cancer Research Patients Committee of La Ligue Nationale contre le Cancer.